STIC-ILL

4148823 10/10/2

From: Ware, Todd 1615
Sent: Wednesday, October 02, 2002 11:18 AM
To: STIC-ILL
Subject: 09/596,362

crave EtOH
to counteract anxiety
if ↓ anxiety ⇒ ↓ EtOH craving

-----Original Message-----
From: Ware, Todd
Sent: Tuesday, October 01, 2002 3:27 PM
To: STIC-ILL
Subject: FW: 09/596,362

Hello

Please send a copy of the following article to me in CM1-2B07

Thank you!
Todd
305-1700

L17 ANSWER 5 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI B.V.
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TI Benzoctamine and oxazepam in the management of alcohol withdrawal states. Comparison by double blind trial.
AU Gillmer R.E.
CS South Africa
SO South African Medical Journal, (1973) 47/47 (2267-2268).
CODEN: SAMJAF
DT Journal
FS 037 Drug Literature Index
032 Psychiatry
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
LA English
AB Alcoholics voluntarily undergoing psychotherapy during alcohol withdrawal were admitted to a double blind trial comparing the anxiolytic and resocializing effects and tolerability of benzoctamine (Tacitin; Ciba) and oxazepam. Thermometer scale reflections of adequacy, aggression, anger, anxiety, tension, drive, mood, insomnia, and craving for alcohol , were recorded and grouped to give a total rating score before treatment and at 3 and 4 weeks. Tolerability was assessed from unsolicited remarks.

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Benzoctamine and Oxazepam in the Management of Alcohol Withdrawal States

COMPARISON BY DOUBLE-BLIND TRIAL*

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SUMMARY

Alcoholics voluntarily undergoing psychotherapy during alcohol withdrawal were admitted to a double-blind trial comparing the anxiolytic and resocializing effects and tolerability of benzoctamine (Tacitin; Ciba) and oxazepam. Thermometer scale reflections of adequacy, aggression, anger, anxiety, tension, drive, mood, insomnia, and craving for alcohol, were recorded and grouped to give a total rating score before treatment and at 3 and 4 weeks. Tolerability was assessed from unsolicited remarks.

S. Afr. Med. J., 47, 2267 (1973).

The trial was conducted at Lulama, a treatment centre in Durban, offering facilities for both in- and outpatients suffering from alcoholism. An extensive multidisciplinary approach provides individual counselling and appropriate psychotherapy, as well as educational programmes, occupational therapy, group sessions, yoga, and relaxation classes. A comprehensive medical and psychiatric service is available and facilities are extended to relatives and ex-patients, in the form of evening programmes devoted to group meetings, and education in aspects of family and social life influential in the development and treatment of alcoholism.

Inpatients are encouraged to remain for 28 days, and in recent years the following medication regimen has been found effective in controlling withdrawal symptoms in most cases:

1. Oxazepam 30 mg *q.i.d.* for 3 days
   Oxazepam 30 mg *t.d.s.* for 11 days
   Oxazepam 15 mg *t.d.s.* for 14 days
2. Phenobarbitone 50 mg with sodium phenytoin 100 mg for 5 days
3. Nitrazepam 5 mg when necessary
4. Vitamin B complex by injection, 2 ml daily for 5 days, and thereafter 1 tablet *t.d.s.*

Previous studies with benzoctamine (Tacitin; Ciba) have shown that it has a significant tranquillizing action and is well tolerated in the recommended average dosage of 10 mg *t.d.s.* Maximal plasma concentrations are achieved within 1 - 2 hours.

Metabolic studies[1] show that benzoctamine is fully absorbed after oral administration; in man, most of the drug is excreted in the urine in the form of inactive metabolites conjugated with glucuronic acid.

* Date received: 28 June 1973.

MATERIALS AND METHODS

Trial Design

Benzoctamine and oxazepam were compared in order to assess the relative ability of the 2 tranquillizers to control the withdrawal symptoms resulting in alcoholics when alcohol is abruptly withdrawn. Thirty-four adult alcoholics were admitted to this study. Patients were allocated blindly to one or the other treatment in accordance with a predetermined random list. Endogenous depression, severe hepatitis, and renal disease were excluded.

Treatments

The 2 comparative medications were made up in identical capsules. The dosages were:

Benzoctamine	2 x 10 mg *q.i.d.*—first	3 days
	2 x 10 mg *t.d.s.*—next	11 days
	1 x 10 mg *t.d.s.*—last	14 days
Oxazepam	2 x 15 mg *q.i.d.*—first	3 days
	2 x 15 mg *t.d.s.*—next	11 days
	1 x 15 mg *t.d.s.*—last	14 days

Methods of Evaluation

Efficacy was assessed independently by the psychiatrist and the patient. A thermometer scale[2] was used. The patients recorded their feelings of adequacy, anger, aggression, anxiety, degree of initiative, severity of insomnia, and craving for alcohol. In addition, the investigator assessed adequacy, anger, aggression, anxiety, mood and restlessness, and recorded on a 5-point scale the global assessment of response.

Assessments were carried out on admission and before the patient had commenced the routine Lulama treatment, and at the end of weeks 2 and 4.

RESULTS

Completed case record forms were obtained for 15 patients on benzoctamine, and for 19 patients on oxazepam. One patient in the benzoctamine group developed convulsions believed to be due to alcohol withdrawal in the first week of treatment, and was dropped from the trial.

Table I gives details of the age and sex distribution of the trial groups and shows that the 2 groups are homogeneous in these respects.

TABLE I. AGE AND SEX DISTRIBUTION

Group	Benzoctamine	Oxazepam
Males	13	13
Females	3	6
Total	16	19
Mean age	43,31	43,84

Scores representing the psychiatrist's assessment of the patient's condition based on the thermometer scales were totalled before treatment and at the end of 2 and 4 weeks. The details appear in Table II.

TABLE II. PSYCHIATRIST'S ASSESSMENT

Week	Benzoctamine	No.	Oxazepam	No.	Diff.
0	40,24±2,2	16	42,58±1,95	19	2,34
2	19,75±1,34	15	25,89±2,73	19	6,14
4	11,93±0,75	15	17,44±2,46	19	5,51

It will be seen from Table II that the initial scores are very similar for the 2 treatment groups. By week 2 benzoctamine had lowered the score to a greater degree than oxazepam, although this trend does not reach statistical significance. However, by week 4 benzoctamine is statistically significantly superior compared with oxazepam in lowering the score. Table III shows the summed-up scores of the variables used and represents the patients' own assessments. It can be seen that although there is no significant difference between the treatments at week 0, in weeks 2 and 4 benzoctamine shows a statistically significant superior effect compared with oxazepam.

TABLE III. PATIENTS' ASSESSMENTS

Week	Benzoctamine	No.	Oxazepam	No.	Diff.
0	29,32±3,49	16	30,69±3,00	19	1,38
2	8,62±1,43	15	16,43±3,17	19	7,81
4	6,46±1,10	15	14,32±2,83	19	7,86

Analysis of the individual measurements showed, according to the investigator's assessment, that benzoctamine was superior at the 5% level to oxazepam in weeks 2 and 4, in 3 out of 6 variables (anger, aggression and mood). Oxazepam was better than benzoctamine in only 1 variable (anxiety), but this was not statistically significant.

According to the patients' scoring, benzoctamine was superior at the 5% level to oxazepam in 3 out of 7 variables (adequacy, anger, aggression), after 2 weeks of treatment, and 4 out of 7 symptoms (anger, aggression, anxiety and the need for alcohol) after 4 weeks' treatment. In none of the 7 variables compared was oxazepam superior to benzoctamine.

The investigator's assessment showed that of the 15 patients completing treatment in the benzoctamine group, and of the 19 patients in the oxazepam group, the response to treatment was excellent in 14 cases in the former group, and 17 in the latter group. Clearly, there is little difference between the 2 groups in the investigator's assessment of response which in the majority of cases was excellent.

Side-Effects

No significant side-effects were encountered in any of the patients. The fact that they were suffering severe alcohol withdrawal symptoms may well have masked minor side-effects.

CONCLUSION

Student's *t*-test applied to the summed scores of the investigator's and patients' ratings, showed benzoctamine to be significantly superior to oxazepam in weeks 2 and 4. Benzoctamine was found by the investigator to be superior in weeks 2 and 4 in improving the feelings of adequacy, anger, aggression, anxiety, mood, and restlessness, although statistical significance was only reached in weeks 2 and 4 for anger, aggression and mood.

An assessment of the patients' scoring showed benzoctamine to be superior to oxazepam in all the variables tested, by weeks 2 and 4. Statistical significance was however only reached for adequacy, anger and aggression, by week 2, and anger, aggression, anxiety, and need for alcohol, by week 4.

I should like to thank Mr R. D. Hutchison, Head of Methodology, Medical Department, Ciba-Geigy (Pty) Ltd, who performed the statistical analysis; Dr Dudley Jacobs, Medical Director, Ciba-Geigy (Pty) Ltd, for advice and guidance; Mrs Winifred Swift, Director of Lulama Treatment Centre, and the Matron and Staff of Lulama Treatment Centre, Durban, for their kind co-operation.

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